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Neurons with large bilateral receptive fields in monkey prelunate gyrus

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Abstract In single-cell recordings from the dorsocaudal part of the prelunate gyrus of an alert monkey (*Macaca fascicularis*) we found neurons with unexpectedly large receptive fields (RFs) that spread bilaterally into the contra- and ipsilateral visual fields. These neurons ($n=82$) appeared to be clustered in the periphery of V4. They were surrounded by neurons with relatively small ($3\text{--}10^\circ$) and unilateral RFs in the contralateral field with properties similar to those previously described for neurons in area V4. Bilateral RFs extended over large parts of the lower visual field but always spared the fovea. Receptive fields typically revealed two foci of maximal responsiveness that were arranged symmetrically in the ipsi- and contralateral fields. Twenty-six cells did not respond to stimuli along the vertical meridian; these neurons had two distinct RFs. The preference for stimulus orientation, color, or motion was similar in all parts of these large RFs.

Keywords Visual cortex · Extrastriate areas · Symmetry · Area V4

Introduction

Anatomical investigations of interhemispheric connections in visual cortical areas have revealed two types of transcallosal projections (Lewis and Olavarria 1995).

The first type links corresponding representations of the vertical meridian in the right and left hemispheres combining anatomically separated representations of the same visual field. The second type connects regions in the right and left visual hemifields that are distant from but nearly symmetrical across the vertical meridian. While the first type of transcallosal fibers is generally found in all cortical visual areas, the distribution of the second type of connections has been shown to depend on the complexity of the visual system. In rats, for example, these fibers have already been seen in area V1 while in cats and monkeys they have been found only in extrastriate cortex (e.g., Maunsell and Van Essen 1987; for review see Lewis and Olavarria 1995). Patches of dense transcallosal projections belonging to the second type have been found in macaque monkeys in the prelunate gyrus, particularly in the region which corresponds to the representation of the periphery of the visual field in area V4. When such connections were first described, it was expected that neurons with bilateral and symmetrical receptive fields (RFs) should be found there in single-cell recordings (Tanaka et al. 1986; Van Essen et al. 1982). However, such neurons were never reported for area V4. The only observed effect of transcallosal fibers in this area was inhibition from the contralateral hemifield (Desimone et al. 1993).

We investigated neuronal responses in V4 in alert monkeys (*Macaca fascicularis*), performing a visual search task. Using a new recording technique (Pigarev et al. 1997b), we performed long tangential penetrations in one animal, which started dorsocaudally in the prelunate gyrus, in the representation of the periphery of the visual field, and passed along the gyrus to the representation of the fovea. In the course of these penetrations we found neurons with large bilateral RFs which often had two separated regions in the contra- and the ipsilateral parts of the visual field (dual RFs). The long penetrations allowed us to investigate their location in the prelunate gyrus and their distribution among neurons with unilateral RFs.

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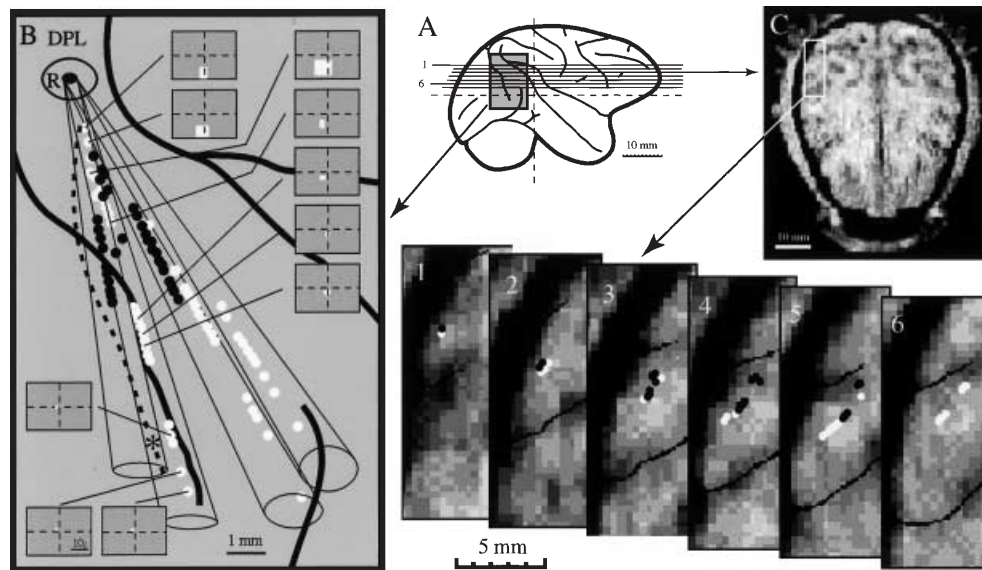


Fig. 1A–C Locations of neurons with unilateral RF (*white dots*) and neurons with bilateral RF (*black dots*) in the prelunate gyrus of the monkey (right hemisphere). **A** Reconstruction of cortical topography based on MRI data. *Horizontal lines* Levels of six brain slices, fragments of which are presented in the *plates 1–6* (borders of the prelunate gyrus emphasized). **B** Enlarged representation of the cortical region outlined in **A**. Cones mark the volume of cortex reached in recordings through guide tubes placed outside the skull. *Dashed line* Approximate representation of the vertical meridian in this part of the gyrus. *Asterisk* Representation of the fovea. Inserts show RF plots at or near the vertical meridian on a sketch of the monitor ($30\times 40^\circ$; *dashed lines* vertical and horizontal meridians). **C** Example of an MRI scan of the third brain slice in **A**. The white rectangle outlines the region enlarged in *plate 3* below

Localization of recording sites in the brain

Because only small holes were drilled into the skull, the prelunate gyrus could not be identified by direct visual inspection, and its location was reconstructed from images taken during magnetic resonance imaging (MRI) sessions. Images were acquired under ketamine anesthesia at a 2.35-T scanner (Bruker Biospec). Using the three-dimensional fast low-angle shot sequence (Frahm et al. 1986), orthogonal 1-mm sections of the head in frontal, sagittal, and horizontal orientations were obtained with external water marks as reference points. Based on these sections, cortical topography was reconstructed in stereotaxic coordinates. The precision of the reconstruction was confirmed in recordings in which the anterior and posterior borders of the prelunate gyrus were localized using electrophysiological criteria (Tanaka et al. 1986).

Location and tilts of penetrations in stereotaxic coordinates and the positions of neurons along electrode trajectories were reconstructed in a three-dimensional computer model, from which recording locations could either be projected on any given plane or marked in different slices of the brain for later superposition on corresponding MRI scans.

Visual stimulation and RF plotting

RFs were investigated with bars of different size, orientation, and color generated on a 19-in. monitor (covering $30\times 40^\circ$ of the visual field) and moved or flashed under the investigator's control. The stimuli that evoked the strongest responses were used to plot RFs. In some cells RFs were larger than the size of the monitor, and only the central borders of the RF could be determined. For a few cells responses were also tested quantitatively by presenting stimuli under computer control at various positions in the visual field.

Stimuli varied in luminance between 1 cd/m^2 (dark blue) and 47 cd/m^2 (green) on a monitor background luminance of 0.5 cd/m^2 . To reduce possible stray light effects some RFs were also tested when screen luminance was increased to 5 cd/m^2 . The room was always diffusely illuminated; the luminance of white walls was measured as 5 cd/m^2 .

Material and methods

Head fixation, surgery, and recording of neuronal activity

The data presented here were collected in one male monkey (*M. fascicularis*). Experiments were started when the animal was 2.5 years old (3.5 kg) and lasted for 2 years. Details of the technique of head fixation, neuronal recording, and reconstruction of the cortical topography have been described in detail elsewhere (Pigarev et al. 1997b). Recordings were made while the monkey's head was fixed with a frame attached to the skull. For recording of eye movements, a search coil was implanted around the cornea of one eye.

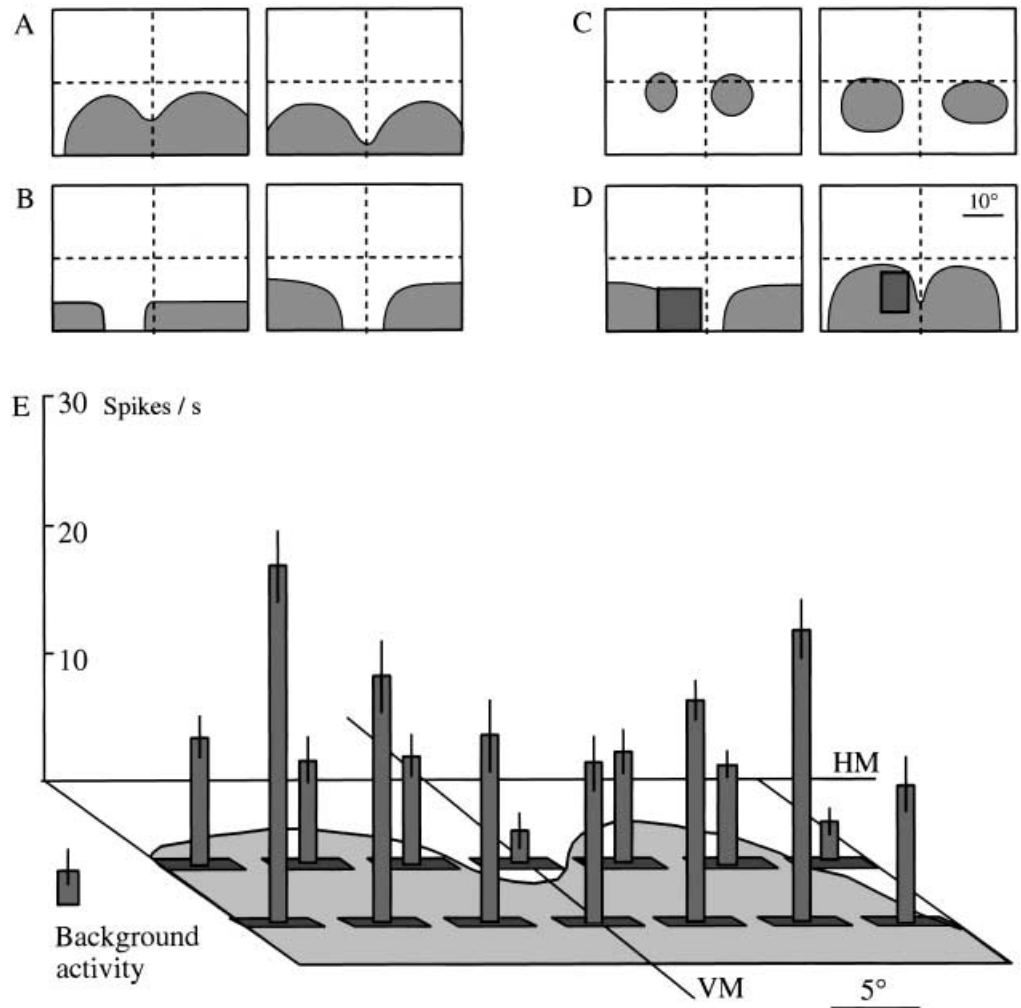
Surgery was performed under general anesthesia with pentobarbital (Nembutal, Sanofi, 5–8 mg/kg intravenously per hour) under aseptic conditions, with postsurgical antibiotic (clindamycin, Sobelin Solubile 300, Upjohn, 20–40 mg/kg three times a day) and analgesic treatment (metamizol, Novalgin, Hoechst, 0.2 ml intramuscularly). All procedures were carried out under institutionally approved protocols and met the NIH guidelines for the care and use of animals.

Varnish-coated tungsten microelectrodes were used for extracellular single cell recordings. Electrodes were inserted into the brain through conic guide tubes and small holes in the skull (1.5 mm; R in Fig. 1B). The conic shape of the guide tubes produced some scatter of possible microelectrode trajectories for each tube orientation (indicated by cones in Fig. 1B). Electrodes were often left in the guide tube after recording sessions so that penetrations could be continued over several days.

Results

In the course of penetrations along the prelunate gyrus we recorded from two types of neurons: cells with small unilateral RFs whose sizes increased with eccentricity (120

Fig. 2A–E Examples of bilateral RFs recorded in the prelunate gyrus. RFs are plotted onto a sketch of the monitor screen (*rectangular outline*). *Broken lines* Vertical and horizontal meridians. **A** Examples of the most frequently encountered RF shapes in neurons with large bilateral RFs. **B,C** Examples of cells with distinct dual bilateral RFs. **D** RF shapes of neurons with bilateral RFs and neurons with unilateral RF, which were recorded simultaneously or after a small shift of the microelectrode in the same experiment. **E** Neuronal responses (*vertical bars*) to a horizontal bar stimulus presented for 500 ms at different locations on the screen, while the monkey fixated a central spot (intersection of the horizontal, *HM*, and vertical, *VM*, meridians). *Gray surface* Shape of the RF as plotted by hand. Each response bar represents the average and the standard error of the mean, of five responses to stimulus presentations at corresponding locations



neurons, white dots in Fig. 1), and cells with large bilateral RFs (82 neurons, black dots). Neurons with unilateral RFs had the typical properties described previously for neurons in area V4 (Desimone and Schein 1987; Desimone et al. 1985; Tanaka et al. 1986; Schein and Desimone 1990; Zeki 1973, 1983). Here we focus on the neurons with large bilateral RFs, which were not described so far.

The RF borders of neurons with bilateral RFs could be determined precisely because these neurons usually responded well to small stimuli, particularly to downward movements of thin vertical bars (width less than 0.5°). Only 17 neurons with large bilateral fields had simple oval RFs; most RFs had a more complex shape. Examples of the most frequently encountered RF type ($n=39$) are shown in Fig. 2A; RFs extended into both hemifields with an interesting shape. Examples of other, less frequently encountered RF shapes are shown in Fig. 2B ($n=10$), and Fig. 2C ($n=16$). For all neurons with bilateral fields RF profiles were such that at least $2\text{--}3^\circ$ of the central visual field was spared.

Usually bilateral RFs had two zones of maximal activation (hotspots), one in the ipsilateral and one in the contralateral visual field. Responses to stimuli presented along or close to the vertical meridian were weaker and could even

be absent. Figure 2E shows averaged responses (vertical columns) of one such neuron to an optimally oriented horizontal bar presented at different positions in the RF.

In some cells, the responses around the vertical meridian were dramatically reduced, leaving clearly unresponsive regions between the two parts of the RF. Twenty-six neurons demonstrated distinct dual bilateral RFs (Fig. 2B, C). Each of these cells had two separate responsive zones located more or less symmetrically in the contra- and the ipsilateral visual fields.

Most of the neurons with bilateral RFs were investigated using binocular stimulation. In three neurons RFs were also studied monocularly. In these neurons the ipsilateral parts of the RF failed to respond to stimulation of the ipsilateral (right) eye alone. However, responses to binocular stimulation were stronger than those to stimulation of the contralateral eye alone. On the other hand, monocular stimuli in the contralateral eye were strong enough to plot the complete RFs and to establish their bilateral structure.

Neurons that responded better to one stimulus than to another did so in all parts of the RF. In particular, the two centers of maximal sensitivity in the RF always revealed similar preferences for the orientation, color, and motion of a stimulus.

Figure 1B shows the recording sites of all neurons in this study projected onto a lateral view of the prelunate gyrus. The neurons with bilateral RFs (black dots) were all located in the superior part of the gyrus and appeared to be clustered in distinct patches that are surrounded by neurons with unilateral RF (white dots). This is also seen in panels 1–6, where the locations of these neurons are superimposed onto horizontal MRI sections of the prelunate gyrus. In the inferior part of the gyrus, in particular in the area of the foveal representation, only neurons with unilateral RF were found.

Neurons with unilateral RF that were located in the inferior part of the gyrus and represented the central visual field and neurons that were located between the patches of neurons with bilateral RFs in the superior part of the gyrus did not differ in their response properties, suggesting that they all belonged to a functionally uniform population. Their mean RF size increased monotonously with RF eccentricity, as has previously been described for V4 neurons (Desimone and Schein 1987; Maguire and Baizer 1984). Thus neurons with unilateral RFs including those located between the patches of neurons with bilateral RFs are likely all located within V4.

The retinotopic organization of neurons with large bilateral fields is difficult to describe. Their RFs often included the vertical meridian. However, since the responsiveness along the vertical meridian was usually reduced, it may be more reasonable to analyze the retinotopic organization of the dual response maxima in their RF. These maxima were typically located at eccentricities of 10–15° and were never seen near the fovea. When the electrodes moved towards the region of foveal representation in the gyrus, the borders of the bilateral RFs also moved towards the horizontal meridian; RF borders of two of these neurons actually reached and crossed the horizontal meridian by 2°. However, even these neurons did not respond to foveal stimulation.

It should be stressed that neurons with bilateral RFs and neurons with unilateral RFs could be recorded simultaneously (Fig. 2D). In none of these cases unilateral RFs touched either the horizontal or the vertical meridian.

Discussion

We found neurons with bilateral, often dual, and unexpectedly large RFs in the dorsocaudal part of the prelunate gyrus. Although the observations were made in only one monkey, and individual variations thus cannot be excluded, neurons with bilateral RFs were found consistently in different recordings and were apparently arranged in an ordered way. They seemed to form clusters that were surrounded by neurons with smaller unilateral RFs.

Dual bilateral RFs: fact or artifact?

It might be argued that our findings were due to optical artifacts such as reflections on the monitor screen. We

have examined the monkey's field of view but did not see any reflections that could explain our observations. To reduce reflections we covered large areas of the monkey's visual field (including the primate chair) with black paper in some recordings. This did not have an effect on the structure of the RF. To minimize stray light effects we used constant (and static) background illumination.

The fact that we recorded small unilateral and large bilateral RFs in the same experiment, and sometimes even simultaneously (Fig. 2D), and that these RFs were also recorded under monocular stimulation strongly argues against optical artifacts, squint, or diplopia as possible sources of bilateral RFs.

It is not clear why neurons with dual bilateral RFs have not been found in previous studies of the prelunate gyrus. One reason may be that most studies have focused on the central representation of V4. In this region we also found exclusively neurons with small and unilateral RFs. It is also possible that, because of anatomical variations in the callosal connections in the prelunate gyrus (Van Essen et al. 1982), neurons with bilateral RFs may sometimes be located deeper in the sulcus, at locations from which it is more difficult to record. Another reason why such neurons were not found in previous studies might be the strong dependence of V4 responses on the alertness of the animal. Under monotonous test conditions neurons with RFs in the visual periphery are more likely to be found to attenuate responses to visual stimulation than neurons in the central representation of V4 (Pigarev et al. 1997a). However, although neurons with dual RFs have not been reported for the cortex of primates, such neurons have been found in cats (Sheplein and Gerchikova 1982).

Neurons with bilateral RFs: dorsal prelunate area or mosaic elements within V4?

Neurons with large bilateral but single RFs have been reported in the dorsocaudal part of the prelunate gyrus (Maguire and Baizer 1984; Mountcastle et al. 1987) and assigned to a separate area named dorsal prelunate area (DPL; Van Essen 1985). However, the neurons with bilateral RFs reported here do not seem to be located in this area. The RFs of neurons in area DPL were not reported to have symmetrical dual structure. In contrast to our findings, the RFs of these neurons often included the fovea and large regions of the upper visual field. Finally, there is an important difference in the topography of the recording site of these neurons compared to ours. We have investigated the area anterior and lateral to the representation of the vertical meridian along the border between V3 and V4, which runs from the anterior wall of the lunate sulcus to the crown of the prelunate gyrus (dashed line in Fig. 1B). By contrast, the neurons attributed to area DPL were located posteromedially from the representation of the vertical meridian (DPL in Fig. 1B; Maguire and Baizer 1984).

Neurons with bilateral RFs described here were located in clusters and had specific response properties that

clearly distinguished them from surrounding neurons. Although this may suggest that they belong to a functionally distinct area, it appears to be more likely that they are mosaic elements within V4. Patchy and mosaic structures have also been found in V1 and V2 of monkeys (Hubel and Livingstone 1985; Livingstone and Hubel 1984a, 1984b; Roe and Ts'o 1995), but they were smaller than those observed here. However, it has been shown that the sizes of mosaic elements are increased in more anterior extrastriate areas (Felleman et al 1997; Pigarev and Rodionova 1995, 1998).

What is the functional role of neurons with dual RFs?

Neurons with dual RFs have been described in several species and neural structures (Kern et al. 1993; Shelepin and Gerchikova 1982; Wylie and Frost 1991; Zenkin and Pigarev 1969). The existence of neurons with similar RFs in visual systems that differ in complexity suggests that these neurons serve important functions in vision.

In pigeons or crabs neurons with bilateral RFs respond to in-phase or anti-phase background movement in the two subregions of their RFs (Kern et al. 1993; Wylie and Frost 1991). In animals with lateral eyes this may help to detect the direction of body movement in the visual environment. However, the neurons with bilateral RFs described in the present study were rarely sensitive to movement, and as with other neurons in V4 (Tanaka et al. 1986), they did not fire especially strong during eye movements. Large bilateral RFs may be useful for the spectral analysis of the general illumination, and may thus contribute to color constancy – a previously described feature of neurons in the prelunate gyrus (Zeki 1980). However, it is not clear what the advantage of symmetrical RFs would be in this case. Another possibility is that these neurons are involved in the transfer of perceptual skills from one hemifield to the other. If so, we would expect to find more effective transfer between corresponding locations of the two hemifields than between noncorresponding locations, as has recently been shown (Ahissar and Hochstein 1996; Harris and Diamond 2000). Finally, neurons with bilateral symmetrical RFs may simply help to detect symmetries in visual patterns, an important feature of visual perception (Tyler 1994). So far the functional role of these neurons remains speculative, and there is no evidence yet to relate any of these effects to the activity of neurons with bilateral RFs as described here. Further investigations are needed to clarify the functions of these neurons.

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